

## REMARKS

Claims 82-84 and 87-94 are pending in the application. No amendments have been made to the claims. Reconsideration of the claims is respectfully requested in view of the following remarks. The Examiner's comments in the final Office Action are addressed below in the order set forth therein.

### The Rejections of the Claims Under 35 U.S.C. §103(a) Should Be Withdrawn

Claims 82-84 and 87-92 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Stomp *et al.* (1999, WO 99/07219) in view of Wong *et al.* (1992, *Plant Molecular Biology* 20:81-93), further in view of Buzby *et al.* (1990, *The Plant Cell* 2:805-814), and further in view of Stiekema *et al.* (1993, *Nucleic Acid Research* 11:8051-8061). This rejection is respectfully traversed.

Independent claim 82 and claims 83-84 and 87-92 directly or indirectly dependent therefrom are drawn to a stably transformed duckweed plant culture or duckweed nodule culture wherein the 5' leader sequence set forth in SEQ ID NO:16 is used in the transformation construct. The use of SEQ ID NO:16 provides for substantial increases in production of recombinant proteins in duckweed that could not have been predicted based upon what was known to those of skill in the art at the time of the present invention.

In support of this position, Applicants have directed the Examiner to the experimental data disclosed in the present application with regard to expression of  $\alpha$ -2b interferon. Tables 3, 4, and 6, on pages 34, 35, and 37, respectively, of the specification show the expression level of  $\alpha$ -2b interferon obtained with the various expression constructs described in Table 2 on page 28 of the specification. The data in these tables demonstrate that very different levels of protein expression are obtained when SEQ ID NO:16 is used as the untranslated leader sequence. In this manner, Applicants have shown that by substituting in the 5' leader sequence from the ribulose-bis-phosphate carboxylase small subunit 5B gene of *Lemna gibba* (SEQ ID NO:16) for the 5'-mas leader in pBMPSP3 (see description of IFN053 construct in Table 2), expression level was increased at least another 10-fold beyond that achieved with construct IFN09 (see Table 6,

comparing the mean average concentration in the media at the 2 week screening trial for construct IFN09 with that obtained for construct IFN53). It is important to recognize that this represents **at least a 10-fold further increase** beyond that observed with the combined optimization and intron modifications of construct IFN09, as the average mean value for construct IFN53 (i.e., 15.3 mg/L) shown in Table 6 is the result of a **one week** growth cycle (compared to a **two week** growth cycle for the other constructs shown in Table 6). Thus, in **one-half the growth time**, the expression construct modified to comprise the 5' leader sequence set forth in SEQ ID NO:16 (construct IFN53) yielded an amount of recombinant protein that was 10-fold greater than the amount of recombinant protein that could be obtained in **twice the time** with the construct comprising the reference 5'-mas leader (construct IFN09).

As previously made of record, the 5' leader sequence set forth in SEQ ID NO:16 has also been shown to enhance the expression of human growth hormone and monoclonal antibodies in duckweed. See pages 38-39 of the specification, Examples 5, 6, and 7. See also, page 55 of Gasdaska *et al.* (2003) *Bioprocessing Journal* 2: 49-56 provided as Cite No. 17 in the Information Disclosure Statement filed September 30, 2003.

Applicants respectfully maintain that this substantial increase in production of recombinant proteins in duckweed could not have been predicted based upon the combined teachings of the cited prior art for all of the reasons of record and further in view of the following remarks.

Stomp *et al.* provide extensive guidance for the transformation of duckweed and provide general guidance regarding the expression of recombinant polypeptides in duckweed. Stomp *et al.* also provide general teachings regarding methods of modifying nucleotide sequences to increase their expression in duckweed. However, Stomp *et al.* do not teach the use of SEQ ID NO:16, as recited in the pending claims, to enhance expression of a biologically active recombinant polypeptide in duckweed.

The Wong *et al.* reference is cited as teaching that the 5' leader from the RbcS gene of *Arabidopsis* can "dramatically enhance expression of a number of heterologous genes" (Office Action mailed February 7, 2008, at page 4, lines 1-2). In maintaining this position, the Examiner concludes that this cited reference teaches that using the 5' UTL of the *Arabidopsis* RbcS gene

results in a 20-fold increase of heterologous gene expression (Office Action at page 4, lines 10-11. Accordingly, the Examiner concludes that Applicants "10 fold increase in expression level is not unexpected" (Office Action at page 4, line 12). Applicants respectfully disagree with this assessment of the predictability of Applicants' experimental results, particularly in view of the teachings of the Wong *et al.* reference.

As an initial matter, Applicants have demonstrated an increase in recombinant protein expression level in duckweed that far exceeds the "10 fold" increase to which the Examiner refers. For example, the expression data for  $\alpha$ -2b interferon described above, and shown in Table 6 at page 37 of the specification, shows that the use of the claimed 5' leader results in a duckweed culture system that is able to produce an average of 15.3 mg  $\alpha$ -2b interferon/L of culture medium when screened after **one week** of culture. In contrast, the use of the reference 5'-mas leader results in a duckweed culture system that is able to produce an average of only 1.5 mg  $\alpha$ -2b interferon/L of culture medium when screened after **two weeks** of culture. Thus, not only does the 5' leader of SEQ ID NO:16 increase the overall amount of recombinant protein production (15.3 mg/L versus 1.5 mg/L), it markedly cuts down the amount of time it takes to yield the increased amount of recombinant protein, i.e., it significantly decreases production time to get 15.3 mg/L of recombinant protein. Therefore, it is inaccurate to state that Applicants have merely demonstrated an expected 10-fold increase in expression level with the use of the 5' leader set forth in SEQ ID NO:16. To the contrary, the fact that the claimed 5' leader sequence dramatically increases yield of heterologous protein while markedly decreasing its production time could not have been predicted based upon the teachings of the cited prior art.

Furthermore, the "20 fold increase" in heterologous protein production with the *Arabidopsis* RbcS 5' leader sequence that the Examiner concludes is taught by Wong *et al.* is a mischaracterization of the data presented in this cited reference. Wong *et al.* investigate the contribution of the *Arabidopsis* RbcS 5' untranslated leader sequence and its associated transit peptide to expression levels of an operably linked CryIA(c) protein in whole tobacco plants, and transient expression levels of this CryIA(c) protein and GUS in tobacco suspension cells. In fact, Wong *et al.* only demonstrate a "20 fold increase" with regard to production of CryIA(c) protein

when the *Arabidopsis* 5' leader sequence **and its associated transit peptide** are operably linked to the CryIA(c) coding sequence. In this manner, Wong *et al.* state:

In this work, expression in transgenic tobacco plants of the *Bacillus thuringiensis* CryIA(c) insecticidal protein under the control of the *Arabidopsis thaliana* Rubisco small subunit *ats1A* promoter with and without transit peptides was compared to expression of the same gene from the CaMV-En35S promoter with and without transit peptide. Results of this study demonstrated that the *ats1A* promoter and untranslated leader directed approximately 20-fold higher levels of *B. thuringiensis* protein expression than the CaMV-En35S promoter when transit peptide coding sequences were included. Levels roughly equal to that of CaMV-En35S were observed when transit peptide was not included with the *ats1A* promoter. . . Our results show that for the *cryIA(c)* gene, **both of these segments** [*ats1A* 5' untranslated leader and transit peptide] are required for maximal expression, and that this effect is observed equally in whole plants and in transient expression assays.

Wong *et al.* at page 91, column 1, "Discussion," paragraph 1, concluding at line 9 of column 2 (emphasis added). In fact, where only the *Arabidopsis* RbcS 5' untranslated leader was included in the construct, regardless of whether the promoter used was the native *ats1A* promoter (whole tobacco plants) or the CaMV-En35S promoter (transient expression assays in tobacco suspension cells), the level of expression of the CryIA(c) protein was essentially the same (in whole tobacco plants) or only slightly higher (in tobacco suspension cells). Thus, for expression in whole tobacco plants, see, for example, the paragraph at column 2, lines 22-26, on page 85 of Wong *et al.*, stating "[l]evels roughly equal to that of CaMV-En35S promoter (pMON5383) were observed **when only the *ats1A* 5' untranslated sequences but not the transit peptide** were included with the *ats1A* promoter" (emphasis added). For the transient expression assays in tobacco suspension cells, see Table 2, column 2, at page 90 of Wong *et al.*, showing less than a 2-fold increase by substitution of the *ats1A* 5' untranslated leader (AL) for the standard polylinker leader (PL) in the *CryIA(c)* expression construct driven by the CaMV-En35S promoter.

In view of their data, Wong *et al.* conclude that "[a] unique feature of the results reported here is that *cryIA(c)* expression was maximally increased **only when both the *ats1A* leader and**

**a translational fusion to the transit peptide were both used** (emphasis added)” (Wong *et al.*, at page 91, column 2, last full sentence on this page).

Wong *et al.* further demonstrate in transient expression assays with tobacco suspension cells that the *ats1A* 5' untranslated leader sequence alone provided for increased expression of GUS. However, even with GUS, in this transient expression assay, the increase in expression with this 5' untranslated leader was only about 6.5-fold (see Table 1 at page 89 of Wong *et al.*). As a result of the discrepancy between the results obtained with GUS and those obtained with Cry1A(c), Wong *et al.* conclude that “the ability of the *ats1A* untranslated leader to increase expression depended on the coding sequence to which it was attached” (see column 1, last sentence before the section entitled “Discussion,” on page 91 of Wong *et al.*).

The results presented by Wong *et al.* teach one of skill in the art that the *Arabidopsis* RbcS 5' untranslated leader may enhance expression of a heterologous protein in **tobacco**, but such enhancement is dependent upon the coding sequence to which this leader sequence is attached, as well as being dependent upon whether or not the native transit peptide must be included in the expression construct to achieve enhanced expression. Where Wong *et al.* teach a 10-fold to 20-fold enhancement of expression, it is only achieved with a construct comprising **both** the RbcS 5' untranslated leader and its native transit peptide. In short, Wong *et al.* teach that the effect of a RbcS 5' untranslated leader on heterologous protein expression is unpredictable. This fact has been acknowledged by the Patent Office, as discussed further herein below.

Applicants have discovered that substantial increases in recombinant protein expression can be achieved in duckweed by including the 5' leader sequence set forth in SEQ ID NO:16 in the transformation construct. This increase in protein expression coupled with the decrease in production time results in a duckweed expression system that provides for unexpectedly high increases in protein production that exceed the 20-fold increase taught by Wong *et al.* Furthermore, Applicants have discovered that this enhanced protein production in duckweed can be obtained with diverse heterologous polypeptides and without a requirement for the native RbcS transit peptide in the expression construct. Such a result could not have been predicted by the teachings of Wong *et al.*

The Buzby *et al.* reference is cited as teaching upstream sequences of three RbcS genes from *L. gibba*, including the 5' leader sequence from the RbcS 5B (SSU5B) gene, which encompasses SEQ ID NO:16. Applicants respectfully note that the focus of Buzby *et al.* is the disclosure of a light-regulated DNA-binding activity that interacts with a conserved region of the *Lemna gibba* SSU5B gene. The authors of this paper have designated this light-regulated DNA-binding activity "light-regulated nuclear factor (LRF-1)" ; see the Abstract on page 1 of this reference. The conserved region of SSU5B with which LRF-1 interacts was identified as being located 150 nucleotides upstream from the transcription start site of this gene, and is delineated by box "X" in Figure 1 at page 807 of this reference (spanning nucleotides -149 to -134 of the 5B sequence). Applicants respectfully note that the 5' leader sequence set forth in SEQ ID NO:16 and recited in the pending claims coincides with nucleotides -1 to +62 of the SSU5B sequence shown in Figure 1 on page 807 of Buzby *et al.* The fact that Buzby *et al.* teach that LRF-1 interacts with a conserved region located approximately 133-148 nucleotides upstream of the claimed 5' leader sequence has no bearing whatsoever on the ability of the claimed 5' leader sequence of SSU5B to enhance expression of an operably linked sequence encoding a heterologous protein that is to be recombinantly produced in duckweed. The markedly enhanced protein production in duckweed obtained with the 5' leader set forth in SEQ ID NO:16 is not taught or suggested by Buzby *et al.* Accordingly, combining the teachings of Buzby *et al.* with those of Stomp *et al.* and Wong *et al.* fails to cure the deficiency of the later two references.

This obviousness rejection also relies on the Stiekema *et al.* reference. Though not addressed in this outstanding Office Action, in the first Office Action dated May 3, 2007, the Examiner cited to Stiekema *et al.* as teaching the *Lemna gibba* transit peptide, and indicated that Stomp *et al.* teach that this transit peptide can be used as a transit polypeptide for enhancing translation. However, Applicants' claimed invention has no requirement for the use of the *Lemna gibba* transit peptide to enhance translation. Rather, the substantial enhancement in protein expression is obtained with the use of the 5' leader sequence set forth in SEQ ID NO:16, which is not a transit peptide. In fact, Applicants have discovered that inclusion of the claimed 5' leader sequence in an expression cassette can advantageously increase heterologous protein production while decreasing production time, without the requirement that this untranslated

leader sequence be operably linked to its native transit peptide. This discovery is not taught or suggested by the combination of Stomp *et al.*, Wong *et al.*, Buzby *et al.*, and Stiekema *et al.*

The Office Action further relies on the teaching of Dai *et al.* (*Transgenic Research* 14:627-643, 2005) as motivation to use the 5' untranslated leader of the *Lemna gibba* RbcS 5B gene as taught by Buzby *et al.* for enhancing heterologous expression of genes in a duckweed plant as taught by Stomp *et al.* (Office Action at page 3, second paragraph). However, Applicants remind the Examiner that a *prima facie* case of obviousness under 35 U.S.C. §103(a) requires that the combination of references places the claimed subject matter in the public domain prior to Applicants' date of invention. See *In re Zenitz*, 333 F.2d 924, 142 USPQ 158 (C.C.P.A. 1964). The publication date of the Dai *et al.* reference post-dates the **April 12, 2005** acceptance date of this research article. The present application has a filing date of **September 30, 2003**. Applicants respectfully note that the post-filing 2005 publication date of the Dai *et al.* reference bars its use as a prior art reference to establish obviousness of the presently claimed invention. See *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1568, 1 USPQ2d 1593, 1597 (Fed. Cir. 1987) ("Before answering Graham's 'content' inquiry, it must be known whether a patent or publication is in the prior art under 35 U.S.C. § 102."). Accordingly, the Examiner's reliance on Dai *et al.* per se to establish the motivation to use the 5' untranslated leader of the RbcS 5B gene from *Lemna gibba* taught in Buzby *et al.* is improper.

The Examiner combines references based on Applicants' disclosure and then argues that the enhanced expression of heterologous proteins in duckweed provided by the 5' leader sequence set forth in SEQ ID NO:16 is not unexpected. This is in direct contrast to the Examiner's assertions in the previous Office Action of May 3, 2007. In that Office Action, the Examiner argued that recombinant protein expression and the use of 5' leader sequences are unpredictable and required that the claims be limited to what was taught in the application. The Examiner argued:

However, the specification does not show enhanced expression by using the 5' leader sequence from the ribulose-bis-phosphate carboxylase small subunit 5B (RbcS) gene of *Lemna gibba* since there is no reference to compare with. Further more, even if the expressions of those proteins were enhanced in duckweed, it still does not enable any other proteins, given the teaching of Wong *et al.* that the ability of 5' untranslated leader sequences and translational fusions to increase gene expression is dependent on the

coding sequences to which you are attached (page 91, 2nd paragraph of right column, lines 7-11).

It is well known in the art that the effect of a 5'-UTL may vary depending on the plant, particularly between dicots and monocots (Dai et al. 2005, Transgenic Research 14:627-643; page 640, 2nd paragraph of left column, lines 8-11). Therefore, undue experimentation would be required to practice the invention in duckweed using 5' leader sequence from RbcS gene of a monocot plant. Furthermore, **even in the same plant of *Lemna gibba*, there are three RbcS genes disclosed by Buzby et al. with 5' leader sequences quite different in sequence (page 807, Figure 1). Only one of them was demonstrated as 5' leader sequence in the working examples.** Silverthorne et al. (1990, Plant Molecular Biology 15:49-58) teach that there are at least [5] RbcS genes in *Lemna gibba* (page 52, figure 1). **Undue experimentation would also be required to determine whether other 5' leader sequences from RbcS genes of *L. gibba* can be used for the instant invention.** Still further, Dai et al. teach that the effect of UTL depend [*sic*]also depends on the promoter it is operably linked. It is found that an overall average of E1 activity in the RA-chl transgenic plants, in which the UTL of AMV RNA4 replaced the UTL of the RbcS-3C, was three times higher E1 transcription and E1 protein accumulation than Rr-chl transgenic plant, whereas when the UTL of the mannopine synthase gene in Mac promoter was replaced with the UTL of AMV RNA4, the E1 protein activity and accumulation in the transgenic plant was 3-4 times lower than that in the Mm-chl transgenic plant (page 640, 2nd paragraph of the left column).

Office Action of May 3, 2007, pages 6-7 (emphasis added).

Accordingly, by the Patent Office's admission, the enhanced expression observed by the use of the 5' leader sequence set forth in SEQ ID NO:16 is unexpected. Thus, the combination of references does not render the claimed invention obvious, and the rejection should be withdrawn.

As the Examiner is aware, establishing a *prima facie* case of obviousness requires assessment of the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), which provides the framework for applying the statutory language of §103. Under the "Graham Factors," the Examiner is required to:

1. Determine the scope and content of the prior art;
2. Ascertain the differences between the prior art and the claims at issue;
3. Resolve the level of ordinary skill in the pertinent art; and
4. Consider any relevant secondary considerations.

Establishing a *prima facie* case of obvious requires that the cited references can be combined such that each and every element of the claimed invention is taught, explicitly or implicitly, by



the references and that a reasonable expectation of success exists in such a combination. In the instant case, Stomp *et al.*, in combination with the other cited references, fail to teach or suggest the use of the 5' leader sequence of SEQ ID NO:16 for production of recombinant proteins in duckweed. It is Applicants who have discovered that this untranslated leader sequence can be used to markedly improve recombinant protein expression in duckweed. Accordingly, Applicants respectfully submit that a *prima facie* case of obviousness has not been established for the pending claims, and further submit that this rejection of the claims should be withdrawn on this basis alone.

Although Applicants do not concede that a *prima facie* case of obviousness has been established for the pending claims, even if established, evidence of secondary considerations such as unexpected results or unforeseen advantageous properties of the claimed invention, including the marked improvement in heterologous protein production as shown here relative to that of the prior art, can rebut a *prima facie* case of obviousness. See *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987); *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). Applicants respectfully remind the Examiner that the secondary consideration of unexpected or superior results obtained with an invention provides objective indicia of nonobviousness. See, for example, *In re Mayne*, 104F.3d 1339, 1342, 41USPQ2d 1451, 1454 (Fed. Cir. 1997) and *In re Woodruff*, 919F.2d 1575, 1578, 16 USPQ2d 1934, 1936-37 (Fed. Cir. 1990).

In view of the secondary consideration of nonobviousness, specifically the unexpected and marked enhancement of expression and recombinant protein production in duckweed that is provided by the claimed invention, the lack of a motivation or reason to combine the Stomp *et al.*, Buzby *et al.*, Stiekema *et al.*, and Wong *et al.* references, and the insufficient guidance provided by the combined teachings of Stomp *et al.* and the other cited references to arrive at the claimed invention, Applicants respectfully request that this rejection of the pending claims under 35 U.S.C. §103(a) be withdrawn.

Claims 82-94 and 87-94 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Stomp *et al.* (1999, WO 99/07219) in view of Wong *et al.* (1992, *Plant Molecular Biology*

20:81-93), further in view of Buzby *et al.* (1990, *The Plant Cell* 2:805-814), further in view of Yu *et al.* (1995, U.S. Patent No. 5460952), further in view of Park *et al.* (1997, *The Journal of Biological Chemistry* 272:6876-6881), and further in view of Stiekema *et al.* (1993, *Nucleic Acid Research* 11:8051-8061). This rejection is respectfully traversed.

As noted above, the Stomp *et al.*, Wong *et al.*, Buzby *et al.*, and Stiekema references fail to demonstrate or even suggest that the 5' leader sequence set forth in SEQ ID NO:16 would be useful for expression of biologically active polypeptides in duckweed. The Yu reference teaches a signal peptide for secretion of a protein into the media of the plant cell cultures. Park teaches that a signal peptide from rice  $\alpha$ -amylase can be recognized and processed by various expression systems. However, neither of these additional references provide the teachings that the 5' leader of the RbcS 5B gene of *Lemna gibba* (SEQ ID NO:16) could be used to markedly enhance recombinant protein production in duckweed. In pointing to his earlier arguments, the Examiner again relies on the teachings of Dai *et al.* as motivation to use the claimed 5' leader sequence for enhancing heterologous protein expression in duckweed. However, as set forth above, the Dai *et al.* reference is not available as prior art for purposes of establishing obviousness. In view of these and the foregoing remarks, Applicants respectfully submit that this rejection of the claims under 35 U.S.C. §103(a) should be withdrawn.

#### The Nonstatutory Double-Patenting Rejections Should Be Withdrawn

Claims 82-84 and 87 were rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-17 of U.S. Patent No. 6,815,184 ('184 patent) in view of Wong *et al.* (1992, *Plant Molecular Biology* 20:81-93) and Buzby *et al.* (1990, *The Plant Cell* 2:805-814). This rejection is respectfully traversed.

The pending claims are directed to a stably transformed duckweed plant culture or duckweed nodule culture wherein the 5' leader sequence set forth in SEQ ID NO:16 is used in the transformation construct. Applicants have shown that this untranslated leader sequence advantageously provides for markedly enhanced recombinant protein production in duckweed, as exemplified by three diverse polypeptides,  $\alpha$ -2b interferon, human growth hormone, and monoclonal antibodies. The '184 patent does not teach the use of this untranslated leader

sequence. Furthermore, neither of the Wong *et al.* and Buzby *et al.* references demonstrates or even suggests that this particular untranslated leader sequence would be useful for expression of biologically active polypeptides in duckweed. Based on the non-obviousness arguments presented above, there was no expectation in the art at the time of Applicants' invention that the claimed leader could be used in duckweed to markedly enhance recombinant protein production. Thus, this rejection of the claims on the ground of nonstatutory obviousness-type double patenting should be withdrawn.

Claims 82-84 and 878-94 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3, 8-10, 23, 26-29 of copending Application No. 10/794,615 ('615 application). This is a provisional rejection because the alleged conflicting claims have not issued as part of a patent.

Applicants respectfully note that the present application and the '615 application are commonly owned. At which time allowable subject matter has been agreed upon, and a double-patenting rejection over this copending application, or a patent issuing there from, is the only remaining rejection barring allowance of the present application, Applicants will address the filing of the terminal disclaimer.

Claims 82-84 and 87 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 11/778,480 ('480 application) in view of Wong *et al.* (1992, *Plant Molecular Biology* 20:81-93) and Buzby *et al.* (1990, *The Plant Cell* 2:805-814). This rejection is respectfully traversed.

As noted above, the pending claims are directed to a stably transformed duckweed plant culture or duckweed nodule culture wherein the 5' leader sequence set forth in SEQ ID NO:16 is used in the transformation construct. Applicants have shown that this untranslated leader sequence advantageously provides for markedly enhanced recombinant protein production in duckweed, as exemplified by three diverse polypeptides,  $\alpha$ -2b interferon, human growth hormone, and monoclonal antibodies. The '480 application does not teach the use of this untranslated leader sequence. Furthermore, neither of the Wong *et al.* and Buzby *et al.*

references demonstrates or even suggests that this particular untranslated leader sequence would be useful for expression of biologically active polypeptides in duckweed. Based on the non-obviousness arguments presented above, there was no expectation in the art at the time of Applicants' invention that the claimed leader could be used in duckweed to markedly enhance recombinant protein production. Thus, this rejection of the claims on the ground of nonstatutory obviousness-type double patenting should be withdrawn.

### CONCLUSION

In view of the foregoing remarks, Applicants respectfully submit that the nonstatutory obviousness-type double patenting rejections and the rejections of the claims under 35 U.S.C. §103 are overcome. Accordingly, Applicants submit that this application is now in condition for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



W. Murray Spruill  
Registration No. 32,943

**CUSTOMER No. 00826**  
**ALSTON & BIRD LLP**  
Bank of America Plaza  
101 South Tryon Street, Suite 4000  
Charlotte, NC 28280-4000  
Tel Raleigh Office (919) 862-2200  
Fax Raleigh Office (919) 862-2260

ELECTRONICALLY FILED USING THE EFS-WEB ELECTRONIC FILING SYSTEM OF THE UNITED STATES PATENT & TRADEMARK OFFICE ON JUNE 9, 2008.  
LEGAL02/30831466v1